PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 11 June 2001 (11.06.01)	
International application No. PCT/GB00/03770	**Applicant's or agent's file reference** N.75428C GCW
International filing date (day/month/year) 02 October 2000 (02.10.00)	**Priority date** (day/month/year) 04 October 1999 (04.10.99)
Applicant CARTER, John	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

02 May 2001 (02.05.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Pascal Piriou
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
N.75428C GCW		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/03770	02/10/2000	04/10/1999
International Patent Classification (IPC) or national classification and IPC A61K33/00		
Applicant CARTER, John		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
02/05/2001	07.02.2002
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Kling, I Telephone No. +49 89 2399 8471

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03770

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-20 as originally filed

Claims, No.:

1-20 as originally filed

Drawings, sheets:

1/3-3/3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-20
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-20
Industrial applicability (IA)	Yes:	Claims	1-20
	No:	Claims	

2. Citations and explanations
   see separate sheet

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The documents cited in the International Search Report are numbered D1 to D7 in the order of their listing in said Search Report. Unless otherwise indicated, reference is made to the passages cited in said Search Report.

D1 discloses compositions comprising assimilable copper, a source of salicylic acid (in form of salicylic acid acetate) and vitamin C for use as a medicament (see in particular Table 2 and the abstract). This teaching anticipates the subject-matter of claims 1, 5, 7, 18 and 19.

D6 discloses compositions comprising assimilable copper, a source of salicylic acid and vitamin C, manganese, iron, zinc in the claimed ranges for use as a medicament (see in particular claim 1 and Tables I and II). This teaching anticipates the subject-matter of claims 1 to 20.

D3 discloses a vitamin supplement for the treatment of cardiac patient comprising several vitamins such as vitamin A, D, E, K, C, acetylsalicylic acid, copper, zinc, magnesium, iron, copper,....

D5 discloses a therapeutic composition which includes L-tryptophan in combination with a salicylate, an ascorbate, calcium, magnesium, copper, pyridoxine, niacin and a carbohydrate such as fructose. The presence of ascorbic acid facilitates hydroxylation of L-tryptophan and the presence of copper facilitates conversion of L-tryptophan into serotonin.

Although D3 does not specifically claim vitamin C, D5 relates to the advantages of including ascorbic acid and copper in therapeutic composition. The combined teaching of D3 and D5 would lead the skilled man to the subject-matter of claims 1 to 20 of the present application.

D2 discloses a composition for oral consumption comprising a base material uniformly

containing a zinc compound and an amino acid, the composition further includes a copper compound being selected from cupric **salicylate**, cupric sulphate, and cupric tartrate,...
This teaching is of particular relevance for claims 1, 3, 5 to 8,10, 13, 14, 17 to 19 which do not involve an inventive step over the teaching of D2 combined with the teaching of D3.

The present application does not satisfy the criterion set forth in Articles 33(2) and 33(3) PCT because the subject-matter of Claims 1 to 20 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT) and does not involve an inventive step (Rule 65(1)(2) PCT).

The current assessment is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the document D4 and D6 cited in the international search report could become relevant to assess whether claims 1 to 20 satisfy the criteria set forth in Article 33(1) PCT.
D4 discloses compositions for oral use containing at least one zinc compound, at least one amino acid, a source of ascorbic acid which does not appreciably associate with zinc ions, and a base material. The compositions provide for slow release of zinc upon dissolution in the mouth. The source of ascorbic acid provides Vitamin C without interacting with zinc and forming unpalatable by-products.
D7 discloses pharmaceutical compositions comprising one or more omega 3-unsaturated fatty acids and/or their derivatives; vitamin E; vitamin C; and acetylsalicylic acid (aspirin).

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
N.75428C GCW		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 00/03770	02/10/2000	04/10/1999
Applicant		
CARTER, John		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established by this Authority to read as follows:

   PHARMACEUTICAL COMPOSITIONS CONTAINING COPPER, SALICYLIC ACID AND VITAMINES C

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [X] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/03770

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K33/34 A61K31/30 A61K31/60 A61K31/375 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DIRIL, N. ET AL: "Investigation of cytotoxic, mutagenic and antimutagenic effects of ascorbic acid, Cu (II) and aspirin by Salmonella mutagenicity assay" TOXICOL. ENVIRON. CHEM. (1995), 52(1-4), 215-220 , XP000992366 abstract; table 2 ---	1,5,8, 18,19
Y	EP 0 842 664 A (GODFREY JOHN C) 20 May 1998 (1998-05-20) claims 3,6; example 1 ---	1,3,5-8, 10,13, 14,17-19
Y	US 5 770 215 A (MOSHYEDI EMIL PAYMAN) 23 June 1998 (1998-06-23) abstract; claim 1 ---	1-20
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 March 2001	02/04/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Gonzalez Ramon, N

1

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/03770

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,X	EP 0 987 021 A (GODFREY JOHN C) 22 March 2000 (2000-03-22) claims 8-10,13,14	1-20
Y	US 4 853 377 A (POLLACK ROBERT L) 1 August 1989 (1989-08-01) abstract column 7 -column 8; claim 3; table 2	1-20
X	US 5 948 443 A (CHRISTAKIS GEORGE ET AL) 7 September 1999 (1999-09-07) claim 1; tables 1,2	1-20
P,Y	DE 198 55 426 A (LANGHOFF WOLFGANG ;LAUMANN UDO (DE)) 8 June 2000 (2000-06-08) abstract	1-20
X	page 4, line 15-35	1,2,4,5, 9,18,20

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 00/03770

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
EP 0842664	A	20-05-1998	US	5897891 A	27-04-1999
			AU	722478 B	03-08-2000
			AU	4525697 A	21-05-1998
			BR	9705484 A	06-04-1999
			JP	10175870 A	30-06-1998
US 5770215	A	23-06-1998	NONE		
EP 0987021	A	22-03-2000	AU	4734999 A	16-03-2000
			BR	9904036 A	26-09-2000
			JP	2000086522 A	28-03-2000
US 4853377	A	01-08-1989	US	4650789 A	17-03-1987
US 5948443	A	07-09-1999	US	5925348 A	20-07-1999
DE 19855426	A	08-06-2000	WO	0032210 A	08-06-2000

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
12 April 2001 (12.04.2001)

PCT

(10) International Publication Number
WO 01/24803 A2

(51) International Patent Classification⁷: A61K 33/00

(21) International Application Number: PCT/GB00/03770

(22) International Filing Date: 2 October 2000 (02.10.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

9923431.2	4 October 1999 (04.10.1999)	GB
0014420.4	13 June 2000 (13.06.2000)	GB

(71) Applicant and
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(74) Agents: WOODS, Geoffrey, Corlett et al.; J.A. Kemp & Co., 14 South Square, Gray's Inn, London WC1R 5LX (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *Without international search report and to be republished upon receipt of that report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/24803 A2

(54) Title: PHARMACEUTICAL COMPOSITIONS AND THEIR USE

(57) Abstract: A composition comprising: (a) a physiologically acceptable source of assimilable copper; (b) a source of salicylic acid or a physiologically acceptable derivative thereof; and (c) vitamin C.

PHARMACEUTICAL COMPOSITIONS AND THEIR USE

This invention relates to pharmaceutical compositions and their use in the treatment of neoplastic disease.

There has long been a demand for a safe and effective treatment of neoplastic disease. WO 84/04922 proposes the use of copper salicylate complexes for this purpose. However, the copper salicylate complexes of WO 84/04922 are not sufficiently effective to be put to widespread use.

It has now unexpectedly been discovered that a composition comprising an assimilable copper compound, a source of salicylic acid or a derivative thereof and vitamin C, is particularly effective in the treatment of neoplastic disease.

The present invention therefore provides a composition comprising:

(a) a physiologically acceptable source of assimilable copper;

(b) a source of salicylic acid or a physiologically acceptable derivative thereof; and

(c) vitamin C.

Addition of vitamin C to components (a) and (b) leads to a synergistic increase in effectiveness.

Preferably, the composition of the invention further comprises (d), a physiologically acceptable source of assimilable manganese. Alternatively, the composition of the invention may further comprise (e), a physiologically acceptable source of assimilable iron or (f), a physiologically acceptable source of assimilable sulfur. Compositions of the invention comprising both (e) and (f) are particularly preferred.

Particularly preferred compositions of the invention are those comprising:

(a) a physiologically acceptable source of assimilable copper;

(b) a source of salicylic acid or a physiologically acceptable derivative thereof;

(c) vitamin C;

(d) a physiologically acceptable source of assimilable manganese;

(e) a physiologically acceptable source of assimilable iron; and

(f) a physiologically acceptable source of assimilable sulfur.

It has also unexpectedly been found that compositions of the invention further comprising a physiologically acceptable source of assimilable zinc are particularly effective in the treatment of sarcomas.

The present invention therefore also provides a composition of the invention, further comprising a physiologically acceptable source of assimilable zinc.

The sources of copper, manganese, iron and zinc used in the composition of the present invention preferably contain the metals in ionic form, e.g. as salts with organic or inorganic acids. However, other metal compounds which provide assimilable sources of the metals, e.g. metal oxides, can also be used.

Thus, a physiologically acceptable source of assimilable copper is typically a copper oxide or a salt of copper with an organic or inorganic acid. A physiologically acceptable source of assimilable manganese is typically a manganese oxide or a salt of manganese with an organic or inorganic acid. A physiologically acceptable source of assimilable iron is typically an iron oxide or a salt of iron with an organic or inorganic acid. A physiologically acceptable source of assimilable zinc is typically a zinc oxide or a salt of zinc with an organic or inorganic acid.

Suitable physiologically acceptable salts of the above metals with organic acids include salts with orotic acid, aspartic acid, gluconic acid, tartaric acid, citric acid, lactic acid, acetic acid, fumaric acid, maleic acid, malic acid, ascorbic acid, succinic acid, benzoic acid, methanesulphonic acid, ethanesulphonic acid, benzenesulphonic acid and p-toluenesulphonic acid . Suitable physiologically acceptable salts of the above metals with inorganic acids include salts with hydrochloric acid, hydrobromic acid, hydriodic acid, phosphoric acid, diphosphoric acid, nitric acid or sulfuric acid, preferably hydrochloric, hydrobromic, hydroiodic, phosphoric or sulfuric acid. Such salts are available commercially or may be prepared if desired by known methods.

Preferred physiologically acceptable salts are salts with organic acids, more preferably salts with orotic acid, aspartic acid, gluconic acid, tartaric acid, citric acid, lactic acid or acetic acid and most preferred are salts with orotic or gluconic acid.

It is also preferred that the physiologically acceptable salts are water soluble, for example salts with gluconic acid.

It is particularly preferred that the physiologically acceptable salt of assimilable copper is copper orotate or copper gluconate, most preferably copper gluconate. It is particularly preferred that the physiologically acceptable salt of assimilable manganese is manganese orotate or manganese gluconate, most preferably manganese gluconate. It is particularly preferred that the physiologically acceptable salt of assimible iron is iron orotate or iron gluconate, most preferably iron gluconate. It is particularly preferred that the physiologically acceptable salt of assimilable zinc is zinc orotate or zinc gluconate, most preferably zinc gluconate.

When, as is preferred, the compositions of the invention contain more than one metal, all the metal salts preferably include the same anion. This anion is typically orotate or gluconate, preferably gluconate.

The source of salicylic acid or a physiologically acceptable derivative thereof is typically salicyclic acid or a physiologically acceptable derivative thereof. Typically, the said derivative is a compound in which the carboxyl or hydroxyl function of salicylic acid has been converted into a derivative.

A physiologically acceptable derivative of salicyclic acid is typically a salicylic acid metal salt, ester or amide. Examples of suitable metal salts include alkali metal salts, for example sodium and potassium salts, and alkaline earth metal salts, for example calcium and magnesium salts. Sodium salicylate is most preferable.

Examples of suitable esters include C_{1-6} alkyl esters, for example methyl, ethyl, propyl, butyl, pentyl or hexyl esters and particularly preferred are the methyl and ethyl esters. Examples of suitable amides are amides obtainable by reacting salicylic acid with an amine HNR_1R_2, wherein R_1 and R_2 may be the same or different and are selected from hydrogen and C_{1-6} alkyl groups such as methyl, ethyl, propyl, butyl, pentyl or hexyl. R_1 and R_2 are preferably selected from hydrogen, methyl and ethyl and most preferably both R_1 and R_2 are hydrogen.

Derivatives in which both the hydroxyl function and the carboxyl function of salicylic acid have been converted into a derivative can also be used.

When the hydroxyl function of salicyclic acid is converted to a derivative it is typically converted to an ester, for example a C_1-C_6 alkyl ester such as acetyl-salicylic acid (aspirin).

A particularly preferred derivative of salicylic acid is sodium salicylate.

Salicylic acid itself and suitable derivatives of it are commercially available.

Components (a) and (b) may be present in the composition of the invention as a copper salicylate complex. As used herein, a copper salicylate complex is a complex of copper and salicylic acid or a complex of copper and a said physiologically acceptable derivative of salicylic acid.

Typically, the physiologically acceptable source of assimilable sulfur is elemental sulfur and any allotropic form of sulfur may be used. Preferably, sulfur is present in the composition in the form of sublimed sulfur or precipitated sulfur, most preferably sublimed sulfur.

The compositions of the invention typically comprise 15 to 60, preferably 25 to 40, parts by weight copper gluconate, or equivalent amount of active ingredient when a physiologically acceptable source of assimilable copper other than copper gluconate is used.

Typically, the compositions of the invention comprise from 300 to 600, preferably 300 to 400, most preferably 350, parts by weight sodium salicylate, or equivalent amount of active ingredient when salicylic acid or a physiologically acceptable derivative thereof other than sodium salicylate is used.

Typically, the compositions of the invention comprise from 200 to 1000, preferably 300 to 500, most preferably 400, parts by weight vitamin C. Preferably, vitamin C is present in the compositions of the invention in an amount significantly larger than that which is regarded as the normal minimum daily requirement for an adult.

Typically, the compositions of the invention containing a physiologically acceptable source of assimilable manganese, comprise from 15 to 60, preferably 25 to 40, parts by weight manganese gluconate, or equivalent amount of active ingredient when a physiologically acceptable source of assimilable manganese other than manganese gluconate is used.

Typically, the compositions of the invention containing a physiologically acceptable source of assimilable iron, comprise from 15 to 60, preferably 25 to 40, parts by weight iron gluconate, or equivalent amount of active ingredient when a physiologically acceptable source of assimilable iron other than iron gluconate is used.

Typically, the compositions of the invention containing a physiologically acceptable source of assimilable sulfur, comprise from 15 to 60, preferably 25 to 40, parts by weight sulfur.

Typically, the compositions of the invention containing a physiologically acceptable source of assimilable zinc, comprise from 15 to 60, preferably 25 to 40, parts by weight zinc gluconate, or equivalent amount of active ingredient when a physiologically acceptable source of assimilable zinc other than zinc gluconate is used.

The parts by weight referred to are based on the total weight of these ingredients in the composition.

The amounts of the active ingredients in the compositions of the invention should be calculated having regard to the intended dosage to be administered. When the composition is to be administered orally, as is usual, a suitable dosage is about 2ml volume for each 60 lbs of body weight of the subject to be treated. This dosage can be administered up to three times a day. The 2ml volume dosage typically contains from 8 to 35 mg, preferably from 14 to 25 mg of copper gluconate, or an equivalent amount of active ingredient when a physiologically acceptable source of copper other than copper gluconate is used. The 2ml volume dosage typically contains from 170 to 350 mg, preferably from 170 to 230 mg and most preferably about 200 mg sodium salicylate or an equivalent amount of active ingredient when salicylic acid or a physiologically acceptable derivative thereof other than sodium salicylate is used. The 2ml volume dosage typically contains from 110 to 570 mg, preferably from 170 to 285 mg and most preferably about 230 mg vitamin C.

A suitable dosage of about 2 ml volume of the compositions of the invention comprising a physiologically acceptable source of assimilable manganese, typically contains from 8 to 35 mg, preferably from 14 to 25 mg of manganese gluconate or an

equivalent amount of active ingredient when a physiologically acceptable source of manganese other than manganese gluconate is used.

A suitable dosage of about 2 ml volume of the compositions of the invention comprising a physiologically acceptable source of assimilable iron typically contains from 8 to 35 mg, preferably from 14 to 25 mg of iron gluconate or an equivalent amount of active ingredient when a physiologically acceptable source of iron other than iron gluconate is used.

A suitable dosage of about 2ml volume of the compositions of the invention comprising a physiologically acceptable source of assimilable sulfur typically contains from 8 to 35 mg, preferably from 14 to 25 mg of sulfur.

A suitable dosage of about 2 ml volume of the compositions of the invention comprising a physiologically acceptable source of assimilable zinc typically contains from 8 to 35 mg, preferably from 14 to 25 mg of zinc gluconate or an equivalent amount of active ingredient when a source of zinc other than zinc gluconate is used.

These figures are approximate and considerable variation in the proportions of the active ingredients is possible without losing the valuable properties of the compositions.

The compositions of the invention may be made by first forming an intimate mixture of the metals to be used in the form of suitable salts or other derivatives, together with sulfur, if present. This mixture in finely ground form can then be added to an aqueous solution or suspension of the salicylic acid or derivative thereof. Typically, from 2 to 5 ml, preferably about 3½ ml of aqueous solution or suspension is used. This solution preferably contains 5-20%, preferably about 10%, by weight of salicylic acid or derivative. The vitamin C may be added before or after the salicylic acid solution, and is preferably added before the salicylic acid solution such that all of the solid ingredients are combined first. The resulting slurry or solution may be administered orally.

The compositions of the invention are thought to work by promoting the formation of the enzyme superoxide dismutase (SOD). SOD functions as a free radical scavenger and reduces DNA damage caused by free radical attack.

The compositions of the invention may be used in human and veterinary

medicine, for example in the treatment of cats and dogs. They are useful in the treatment or prevention of a neoplastic disease. They are capable of improving the condition of a patient suffering from a cancer.

Typically, a human or animal is treated by initially administering said dosage of 2 ml of the composition of the invention, comprising active ingredients in the amounts set out above, in the form of an aqueous solution or suspension, per 60 lbs body weight of subject followed by a half dose of a similar solution or suspension 1 to 2 hours later. Four hours later a further half dose may be given. Subsequent treatment (when the tumour has noticeably regressed and/or the symptoms have been considerably alleviated) may consist of the oral administration of 2 ml of the said solution or suspension per 60 lbs body weight of subject once a day. This may be given for three weeks, then, if further progress has been made, the dose may be reduced to 2 ml per 60 lbs body weight on alternate days for 3 weeks. The frequency of dosing may be further reduced as further progress is made.

The compositions of the invention have been found effective in treatment of carcinomas of the breast, rectum, bladder, liver, peritoneum, stomach and urethra, and in some lymphomas. Compositions of the invention comprising a physiologically acceptable source of assimilable zinc are effective against sarcomas. The treatment may be continued until there is a marked regression in the size of the tumour or until the tumour disappears.

The compositions of the invention are normally administered orally. Preferably, therefore they are suitable for oral administration. Suitable forms for oral administration include, for example, tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules. Preferred forms for oral administration are tablets and capsules. However, other routes of administration may be possible provided suitable precautions are taken to make the compositions suitable for administration in the contemplated way. For example, the compositions of the invention may be administered parenterally, whether subcutaneously, intravenously, intramuscularly, intrasternally, transdermally or by infusion techniques, or as a suppository.

It has been found that the effectiveness of the compositions of the invention

can be enhanced if they are administered in conjunction with a dietary regime which is low in salt and high in potassium and essential amino acids such as proline, serine, glutamine, lysine, histidine, alanine, methionine and leucine. By way of example, vegetables and fruit may be mentioned as foods which have high potassium content. Porridge oats, for example, have a high potassium, low salt content. By way of example, liver may be mentioned as a food source rich in essential amino acids. Typically, for a human patient about 2 oz of liver per day has been found to be sufficient.

It has been found also that better results are obtained by supplementing the diet of a subject with additional vitamin C, i.e. vitamin C in addition to that preferably contained in the compositions of the invention. For example, the administration of 1 g of vitamin C per 20 lbs subject body weight per day, has been found to enhance the activity of the new compositions. Likewise, administration of nicotinic acid, for example 25 mg per 14 lbs subject body weight per day, has been found to give rise to improved activity of the compositions of the invention.

The following Examples illustrate the invention.

EXAMPLE 1

Copper (II) orotate (35 mg) and manganese (II) orotate (35 mg), in finely divided form were mixed dry. Sodium salicylate solution (3.5 ml of a 10% aqueous solution) was then added followed by vitamin C (400 mg). The resulting suspension is suitable for immediate oral administration.

EXAMPLE 2

Copper (II) orotate (35 mg), manganese (II) orotate (35 mg) and zinc orotate (35 mg) in finely divided form were mixed dry. 3.5 ml of a 10% aqueous solution of sodium salicylate (i.e. 3.5 ml of an aqueous solution containing 350 mg sodium salicylate) was then added followed by vitamin C (400 mg). The resulting suspension is suitable for immediate oral administration.

EXAMPLE 3

To copper (II) orotate (35 mg) in finely divided form was added sodium salicylate solution (3.5 ml of a 10% aqueous solution) followed by vitamin C (400 mg). The resulting suspension is suitable for immediate oral administration.

EXAMPLE 4

Copper (II) orotate (35 mg), manganese (II) orotate (35 mg), iron (II) orotate (35 mg) and sublimed sulfur (35 mg), in finely divided form were mixed dry. Sodium salicylate solution (3.5 ml of a 10% aqueous solution) was then added followed by vitamin C (400 mg). The resulting suspension is suitable for immediate oral administration.

EXAMPLE 5

Copper (II) orotate (35 mg), manganese (II) orotate (35 mg), iron (II) orotate (35mg), sublimed sulfur (35mg) and zinc orotate (35 mg) in finely divided form were mixed dry. 3.5 ml of a 10% aqueous solution of sodium salicylate (i.e. 3.5 ml of an aqueous solution containing 350 mg sodium salicylate) was then added followed by

vitamin C (400 mg). The resulting suspension is suitable for immediate oral administration.

EXAMPLE 6

Copper (II) gluconate (35 mg),vitamin C (400 mg) and manganese (II) gluconate (35 mg), in finely divided form were mixed dry. Sodium salicylate solution (3.5 ml of a 10% aqueous solution) was then added. The resulting solution is suitable for immediate oral administration.

EXAMPLE 7

Copper (II) gluconate (35 mg), vitamin C (400 mg), manganese (II) gluconate (35 mg) and zinc gluconate (35 mg) in finely divided form were mixed dry. 3.5 ml of a 10% aqueous solution of sodium salicylate (i.e. 3.5 ml of an aqueous solution containing 350 mg sodium salicylate) was then added. The resulting solution is suitable for immediate oral administration.

EXAMPLE 8

To copper (II) gluconate (35 mg) and vitamin C (400 mg) in finely divided form was added sodium salicylate solution (3.5 ml of a 10% aqueous solution). The resulting solution is suitable for immediate oral administration.

EXAMPLE 9

Copper (II) gluconate (35 mg), vitamin C (400 mg), manganese (II) gluconate (35 mg), iron (II) gluconate (35 mg) and sublimed sulfur (35 mg), in finely divided form were mixed dry. Sodium salicylate solution (3.5 ml of a 10% aqueous solution) was then added. The resulting suspension is suitable for immediate oral administration.

EXAMPLE 10

Copper (II) gluconate (35 mg), vitamin C (400 mg), manganese (II) gluconate (35 mg), iron (II) gluconate (35mg), sublimed sulfur (35mg) and zinc gluconate (35 mg) in finely divided form were mixed dry. 3.5 ml of a 10% aqueous solution of

sodium salicylate (i.e. 3.5 ml of an aqueous solution containing 350 mg sodium salicylate) was then added. The resulting suspension is suitable for immediate oral administration.

EXAMPLE 11

This experiment was conducted at University College London under Home Office License. In this experiment 100 C57B1 male mice were injected subcutaneously with a transplantable RMA thymoma tumour. 50 of the mice were used as controls and 50 mice were experimental mice.

Mice have a much faster rate of metabolism than larger mammals. It was therefore decided to give the mice a larger dose of the formula than the dose which would be suitable for larger animals such as cats and dogs. This latter dose was accordingly increased by a factor of 10.

For a 30 g mouse, 0.022 ml of the solution prepared in Example 1 was administered. This was administered to the mice three times a day at 10 am, 3 pm and 6 pm. The composition was administered by gavage. In addition the experimental mice were fed on a diet of organic wheat, barley, oats and rye.

The general condition of the experimental and control mice following tumour injection is shown in Table 1.

Table 1

RMA thymoma in C57B1 male mice		
Days after Tumour injection	**Control**	**Experimental**
16	All mice have tumours. 2 killed because of large tumour size.	20/22 with palpable tumours. 2 probably have deep tumours. 1 sick mouse killed.
18		3 mice died as a result of treatment. 2 with small tumours. 1 had only a large lymph node.
20	4 mice killed with large tumours.	2 sick mice killed, both had tumours.
21	Remaining mice killed because of large tumours. All tumours firm and infiltrating muscle of thigh or peritoneal wall.	4 killed with large infiltrating tumours.
23		3/12 mice had superficial freely mobile plaque like tumours.
25		6 mice killed because of large tumour size. All tumours firm and infiltrating. 1 mouse had an axillary abscess.
29		4/6 remaining tumours fixed. Large lymph nodes palpable.
31		Remaining mice killed. 5/6 tumours infiltrating deeply. 1/6 more superficial but draining node grossly enlarged.

The growth of the tumour in experimental and control mice is shown in Figure 1. The weights of the experimental and control mice are shown in Figure 2.

The growth of the thymoma tumour was measured by callipers, i.e. the diameter of the surface of the tumour was determined. The tumours were not

weighed at the end of the experiment.

As can be seen from Figure 1, 21 days after tumour injection the tumours in the control mice were approximately 1.9 times larger than those in the experimental mice.

Apart from deaths caused by the stress of gavage, to which the control mice were not subjected, the only side effect observed was slight weight loss, probably attributable to the change of diet.

EXAMPLE 12

This experiment was conducted at University College London under Home Office License. Transplantable mammary carcinomas were injected into 100 male Balb/c mice. 50 of the mice were used as controls and 50 mice were experimental mice.

These tumours grew much more slowly than the thymomas injected in Example 11. Accordingly, less treatment was given to the experimental mice; they were gavaged only once a day with 0.22 ml of the solution prepared in Example 1 and fed on a diet of organic grains as described in Example 11. Nevertheless a result was obtained as can be seen from Figure 3 showing the growth of the mammary carcinoma in experimental and control mice. But because they were given less treatment the difference in growth rate between the experimental and control groups is much less than that observed in Example 11.

The tumours in the control group were only 1.14 times larger than in the experimental group at 23 days after tumour injection. However, 29 days after tumour injection the tumours in the control group were 1.19 times larger than the tumours in the experimental group.

Apart from deaths caused by the stress of gavage, to which the control mice were not subjected, the only side effect observed was slight weight loss, probably attributable to the change of diet.

EXAMPLE 13

Professor Peter Beverley of the Department of Oncology at University College London Medical School stated that although there was a statistically higher significant effect in tumour growth between the experimental and control mice in Examples 11 and 12, it was clear that the treatment by repeated gavage was stressful so that untreated mice were not a perfect control.

It was therefore decided that a further experiment should be performed but that this time the formula should be administered in the drinking water and given to the mice by gavage only once a day. As a water soluble copper salt was required for addition to the drinking water, it was decided to use copper gluconate in place of copper orotate. The control mice would also have the same organic grains diet as the experimental mice and be gavaged with water once a day. It was also decided that the experimental mice should be given extra vitamin C by having the vitamin C added to their drinking water.

This experiment was conducted at University College London under Home Office License.

Copper (II) gluconate, 35 mg, and manganese (II) orotate, 35 mg, in finely divided form were mixed dry. Sodium salicylate solution (3.5 ml of a 10% aqueous solution) was then added followed by vitamin C (400 mg).

The vitamin C was added to the drinking water of the experimental mice by putting 300 mg of vitamin C in 50 ml of water three times a day. Thus each cc contained 6 mg vitamin C. Each mouse drank on average 4 ml of water containing 24 mg of vitamin C three times a day. So each mouse received on average 72 mg of vitamin C per day.

50 C57B1 male mice were injected subcutaneously with a transplantable thymoma. 24 mice, the experimental mice, were treated, and 26 mice were used as a control.

It was decided to give the mice a larger dose of the formula because they would be gavaged only once a day and it was not sure how much drinking water each mouse would drink.

The dose per mouse compared to larger mammals was now increased by a

factor of 17.

Each mouse was gavaged with 0.04 ml of the composition prepared above once a day.

0.5 ml of the composition prepared above was added to the drinking water three times a day. 50 ml of drinking water was provided three times a day. 0.5 ml in 50 ml is 0.01 ml per cc. Each mouse drank approximately 4 ml of water three times a day so each mouse received approximately 0.04 ml of the composition in their drinking water three times a day. Each mouse therefore received approximately a total of 0.04 x 3 = 0.12 ml of the composition from the drinking water each day plus 0.04 ml from the gavage, a total of 0.16 ml per day.

During the trial 4 mice from the experimental group and 5 from the control group died because of the gavage. The mice were all killed on day 17 and the tumours were dissected out and weighed. However, two tumours from the control group could not be removed for measurement because they were too extensive. The results are shown in Table 2.

Table 2

EXPERIMENTAL GROUP		CONTROL GROUP	
Mouse No.	Tumour Weight (g)	Mouse No.	Tumour Weight (g)
1	.10	20	.40
2	.10	21	.50
3	.20	22	.50
4	.20	23	.60
5	.20	24	.60
6	.30	25	.90
7	.30	26	.90
8	.40	27	.90
9	.40	28	1.00
10	.40	29	1.00
11	.50	30	1.00
12	.50	31	1.10
13	.50	32	1.10
14	.50	33	1.30
15	.50	34	1.30
16	.60	35	1.30
17	.70	36	1.50
18	1.00	37	1.70
19	1.70	38	1.80
Average tumour weight	0.48g	39	1.80
		Average tumour weight	1.1

It can be seen from Table 2 that the combined weight of tumours from the experimental group was 9.1 grams. The combined weight of the tumours from the control group was 21.2 grams. The control group tumour mass was therefore 21.2/9.1 = 2.32 times larger than the experimental group tumour mass.

Further, the average tumour weight in the control mice was 1.1 g. The average tumour weight in the experimental mice was 0.48g.

The average control group tumour mass is therefore 1.1/0.48 = 2.29 times larger than the average experimental group tumour mass.

The difference in the size of the tumours as measured by callipers during the trial is shown in Figure 5. It can be seen from Figure 5 that by day 17 the difference in size between the control and experimental tumours, as measured by callipers, is 8.8/3.6 = 2.44 times larger. Again there were no detectable side effects.

Professor Beverley has stated that this experiment has confirmed unequivocally that the treatment causes a statistically highly significant difference in tumour growth between the treated and control mice with no detectable side effects.

EXAMPLE 14

A 30lb 6 year old Manchester Terrier suffering from a spindle cell tumour was treated with the composition described in Example 1.

Before the treatment the animal had a hard lumpy swelling extending over the external side of the left foreleg from below the elbow joint up to the side of the shoulder. This diagnosis was made by Abbey Veterinary Clinics, London, who recommended amputation of the foreleg. 1cc of the composition was administered orally once a day for 5 days. By the end of 5 days the tumour had reduced in size considerably. The dose was then reduced to 1cc on alternate days for a further 7 days.

In addition, an extra 3 g vitamin C was administered orally every day and nicotinic acid was administered orally in an amount of 125mg per day.

A dietary regime was followed of organic fruits, organic vegetables, organic grains and lamb's liver to supply essential amino acids. Salt added to food was avoided.

Following the above treatment, the tumour disappeared. This result was

certified by Mr. A. Sebesteny, head vet at the Imperial Cancer Research Fund, Clare Hall Laboratories.

EXAMPLE 15

A 60lb, 11 year old Doberman bitch was treated with a composition consisting of 30 mg copper orotate, 30 mg manganese orotate, 400 mg vitamin C and 3½ ml of an aqueous solution containing 350 mg sodium salicylate, prepared as in Example 1.

The animal was suffering from a urethral obstruction caused by an infiltrating malignant neoplasm thought to be a transitional cell carcinoma. This diagnosis was made at the department of Clinical Veterinary Medicine, Cambridge University. Before the treatment it could pass only a few drops of water with intense straining.

On the first day of treatment, the animal was given 2cc of the above composition (administered orally). On the second day it was given 2cc, followed by 1cc an hour later, then ½cc an hour after that. This was repeated every day for a week, after which time an improvement was noted. The dosage was then reduced to 2cc once a day for a further 3 weeks.

In addition, an extra 6 g vitamin C was administered orally every day and nicotinic acid was administered orally in an amount of 250 mg per day. A dietary regime as set out in Example 14 was followed.

Following the above treatment, the animal showed none of the former symptoms. It was still alive and in excellent health 4 years after the treatment, as can be confirmed by its owner.

EXAMPLE 16

An 80lb, 6 year old Alsatian was treated with a composition consisting of 50 mg copper orotate, 50 mg manganese orotate, 50 mg zinc orotate, 400 mg vitamin C and 3½ ml of an aqueous solution containing 350 mg sodium salicylate, prepared in the same way as in Example 1, except that the zinc orotate was mixed dry in finely divided form together with the copper and manganese orotate.

The animal was suffering from a nasal tumour, thought to be a sarcoma and

could not breathe through its nose. This diagnosis was made by the Department of Small Animal Medicine and Surgery, Royal Veterinary College, London. It had a large, hard, golf-ball sized swelling under the right eye.

It was given 2.6cc of the above composition, followed by 1.3cc an hour later (administered orally). This dose was repeated daily for 2 weeks by which time the tumour had significantly regressed, to the extent that the animal could breathe through its nose. The dosage was then reduced to alternate days for a fortnight, then to twice a week, then once a week.

In addition, an extra 8 g vitamin C was administered orally every day and nicotinic acid was administered orally in an amount of 330 mg per day.

A dietary regime as set out in Example 14 was followed.

By the end of the above treatment, the animal was symptom free. This result was certified by Mr. A. Sebesteny, head vet at the Imperial Cancer Research Fund.

EXAMPLE 17

A 60lb, 7 year old Doberman dog was treated with the composition described in Example 15. It was suffering from carcinoma of the peritoneum. This diagnosis was made by the Department of Small Animal Medicine and Surgery, Royal Veterinary College, London. The animal was in an emaciated state, with a large swelling on the abdomen.

It was treated with 2cc of the composition, followed by 1cc an hour later (administered orally) every day for two weeks. After two weeks, the dosage was reduced to 2cc per day for a further two weeks, followed by a further reduction to 2cc on alternate days for another two weeks.

In addition, an extra 6 g vitamin C was administered orally each day and nicotinic acid was administered orally in an amount of 250 mg per day.

A dietary regime as set out in Example 14 was followed. After the above treatment the animal was symptom free, as can be confirmed by its owners.

EXAMPLE 18

A 150 lb human male around 45 years old, was treated with the composition

described in Example 15. He was suffering from T-cell lymphoma, diagnosed at the Cromwell Hospital, London.

He was given 4.5cc of the composition (administered orally) once a day for 6 weeks (excluding Sundays). After this time, a regression was noted and the dosage was reduced to alternate days for 2 weeks, followed by a further reduction to once a week for three weeks.

In addition, an extra 15 g of vitamin C was administered orally every day and nicotinic acid was administered orally in an amount of 625 g per day.

A dietary regime as set out in Example 14 was followed. Following the above treatment, all symptoms disappeared. He is still alive and well 6 years after the treatment.

CLAIMS

1. A composition comprising:

(a) a physiologically acceptable source of assimilable copper;

(b) a source of salicylic acid or a physiologically acceptable derivative thereof; and

(c) vitamin C.

2. A composition according to claim 1, further comprising (d) a physiologically acceptable source of assimilable manganese.

3. A composition according to claim 1 or 2, further comprising (e) a physiologically acceptable source of assimilable iron and (f) a physiologically acceptable source of assimilable sulfur.

4. A composition according to any one of the preceding claims, further comprising a physiologically acceptable source of assimilable zinc.

5. A composition according to any one of the preceding claims, wherein the said metals are present in the form of salts with organic or inorganic acids.

6. A composition according to any one of the preceding claims, in which components (a) and (b) are present as a copper salicylate complex.

7. A composition according to claim 5, wherein the salts are the same or different and are selected from orotates, aspartates, gluconates, tartrates, citrates, lactates and acetates.

8. A composition according to claim 5 wherein the salts are the same or different and are selected from chlorides, bromides, iodides, phosphates and sulphates.

9. A composition according to any one of the preceding claims wherein the derivative of salicylic acid is sodium salicylate.

10. A composition according to any one of the preceding claims comprising:

(a) 15 to 60 parts by weight copper gluconate, or equivalent amount of active ingredient when a physiologically acceptable source of assimilable copper other than copper gluconate is used;

(b) 300 to 600 parts by weight sodium salicylate, or equivalent amount of active ingredient when salicylic acid or a physiologically acceptable derivative thereof other than sodium salicylate is used; and

(c) 200 to 1000 parts by weight vitamin C.

the parts by weight referred to being based on the total weight of these ingredients in the composition.

11. A composition according to claim 10, further comprising 15 to 60 parts by weight manganese gluconate, or equivalent amount of active ingredient when a physiologically acceptable source of assimilable manganese other than manganese gluconate is used.

12. A composition according to claim 10 or claim 11, further comprising 15 to 60 parts by weight of iron gluconate, or equivalent amount of active ingredient when a physiologically acceptable source of assimilable iron other than iron gluconate is used, and 15 to 60 parts by weight of sulfur.

13. A composition according to any one of claims 10 to 12, further comprising 15 to 60 parts by weight zinc gluconate, or equivalent amount of active ingredient when a physiologically acceptable source of assimilable zinc other than zinc gluconate is used.

14. A composition according to claim 10, comprising:

(a) 25 to 40 parts by weight copper gluconate, or equivalent amount of active ingredient when a physiologically acceptable source of assimilable copper other than copper gluconate is used;

(b) 350 parts by weight sodium salicylate, or equivalent amount of active ingredient when salicylic acid or a physiologically acceptable derivative thereof other than sodium salicylate is used; and

(c) 400 parts by weight vitamin C.

the parts by weight referred to being based on the total weight of these ingredients in the composition.

15. A composition according to claim 14, further comprising 25 to 40 parts by weight manganese gluconate, or equivalent amount of active ingredient when a physiologically acceptable source of assimilable manganese other than

manganese gluconate is used.

16. A composition according to claim 14 or claim 15, further comprising 25 to 40 parts by weight of iron gluconate, or equivalent amount of active ingredient when a physiologically acceptable source of assimilable iron other than iron gluconate is used, and 25 to 40 parts by weight of sulfur.

17. A composition according to any one of claims 14 to 16, further comprising 25 to 40 parts by weight zinc gluconate, or equivalent amount of active ingredient when a physiologically acceptable source of assimilable zinc other than zinc gluconate is used.

18. A composition according to any one of the preceding claims for use in the treatment of the human or animal body.

19. Use of a composition according to any one of claims 1 to 17 in the manufacture of a medicament for use in the treatment or prevention of a neoplastic disease.

20. Products containing:

(a) a composition as claimed in any one of claims 1 to 17; and

(b) vitamin C and/or one or more amino acids and/or nicotinic acid,

as a combined preparation for simultaneous, separate or sequential use in the treatment of neoplastic disease.

Fig.1.

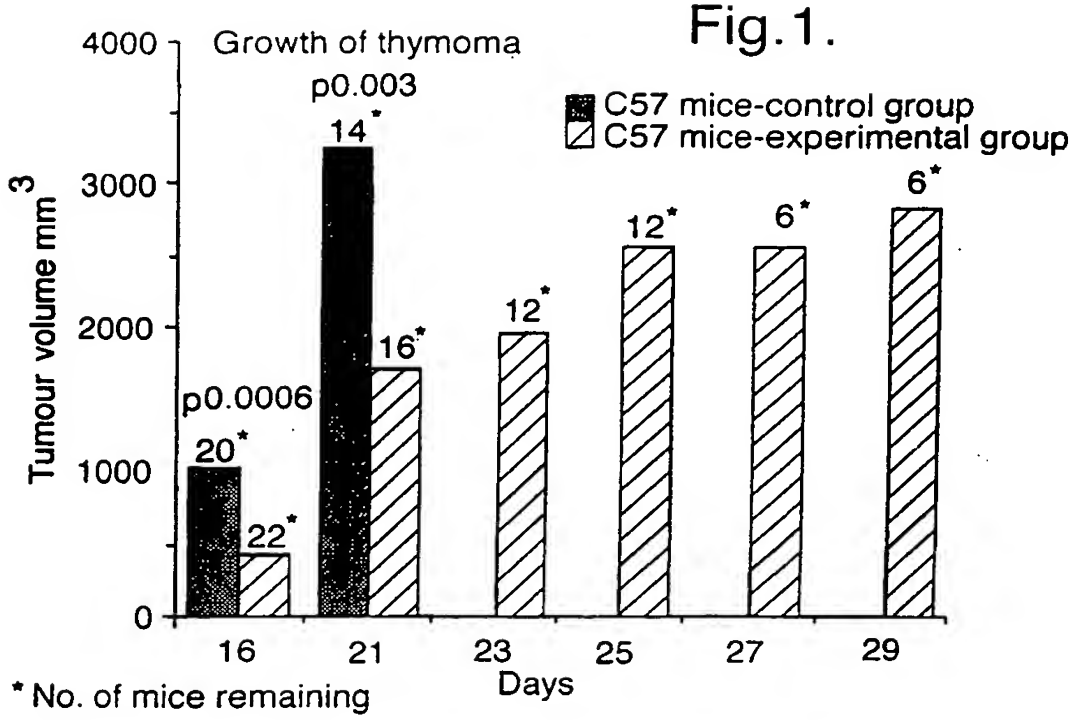

Growth of thymoma
p0.003
p0.0006
C57 mice-control group
C57 mice-experimental group
Tumour volume mm 3
4000
3000
2000
1000
0
20*
22*
14*
16*
12*
12*
6*
6*
16
21
23
25
27
29
Days
* No. of mice remaining

Fig.2.

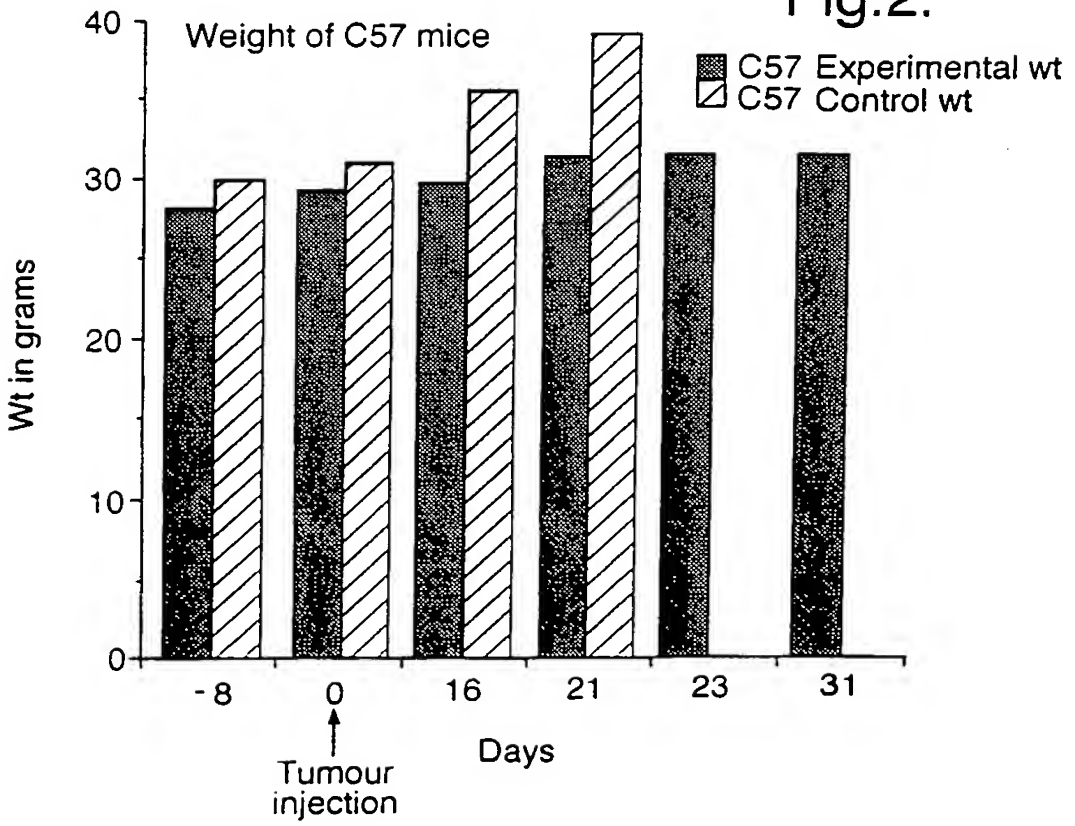

Weight of C57 mice
C57 Experimental wt
C57 Control wt
Wt in grams
40
30
20
10
0
-8
0
16
21
23
31
Days
Tumour injection

Fig.3.

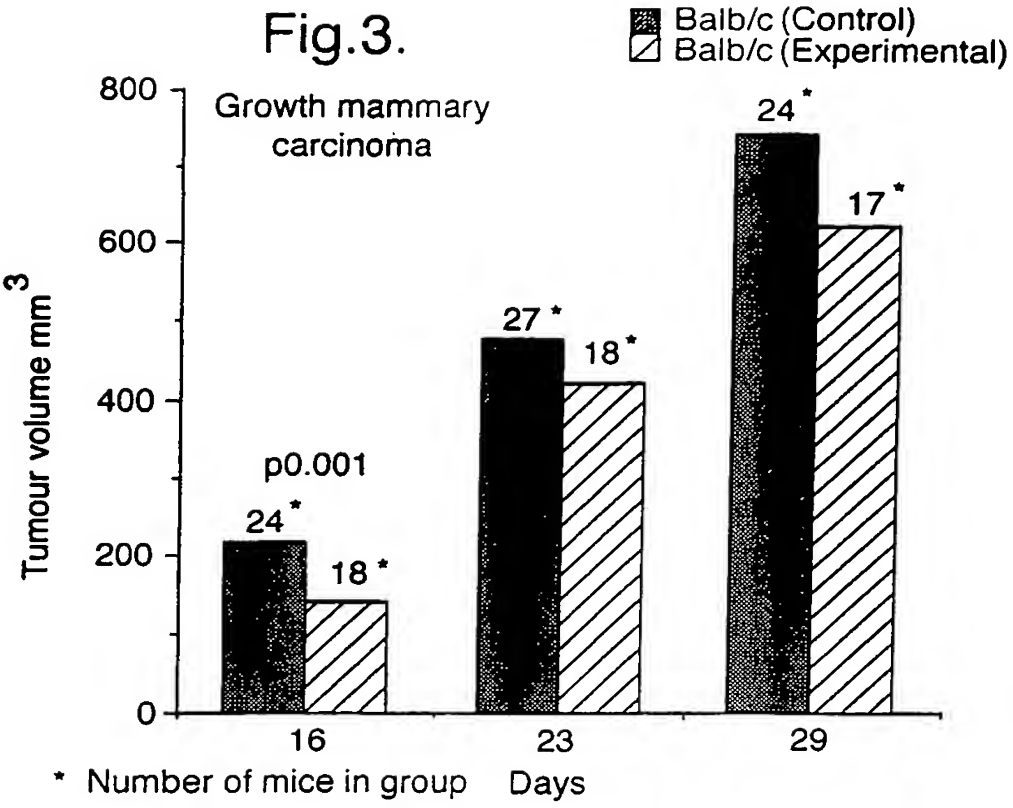
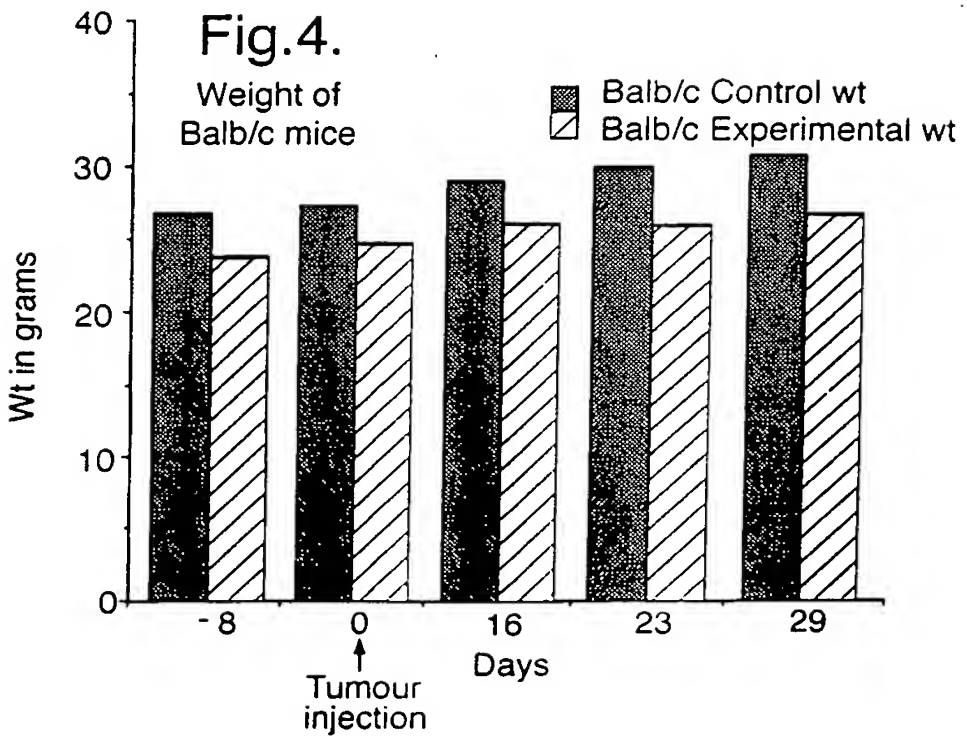

Balb/c (Control)
Balb/c (Experimental)
Growth mammary carcinoma
Tumour volume mm3
800
600
400
200
0
p0.001
24*
18*
27*
18*
24*
17*
16
23
29
* Number of mice in group
Days

Fig.4.


Weight of Balb/c mice
Balb/c Control wt
Balb/c Experimental wt
Wt in grams
40
30
20
10
0
-8
0
16
23
29
Days
Tumour injection

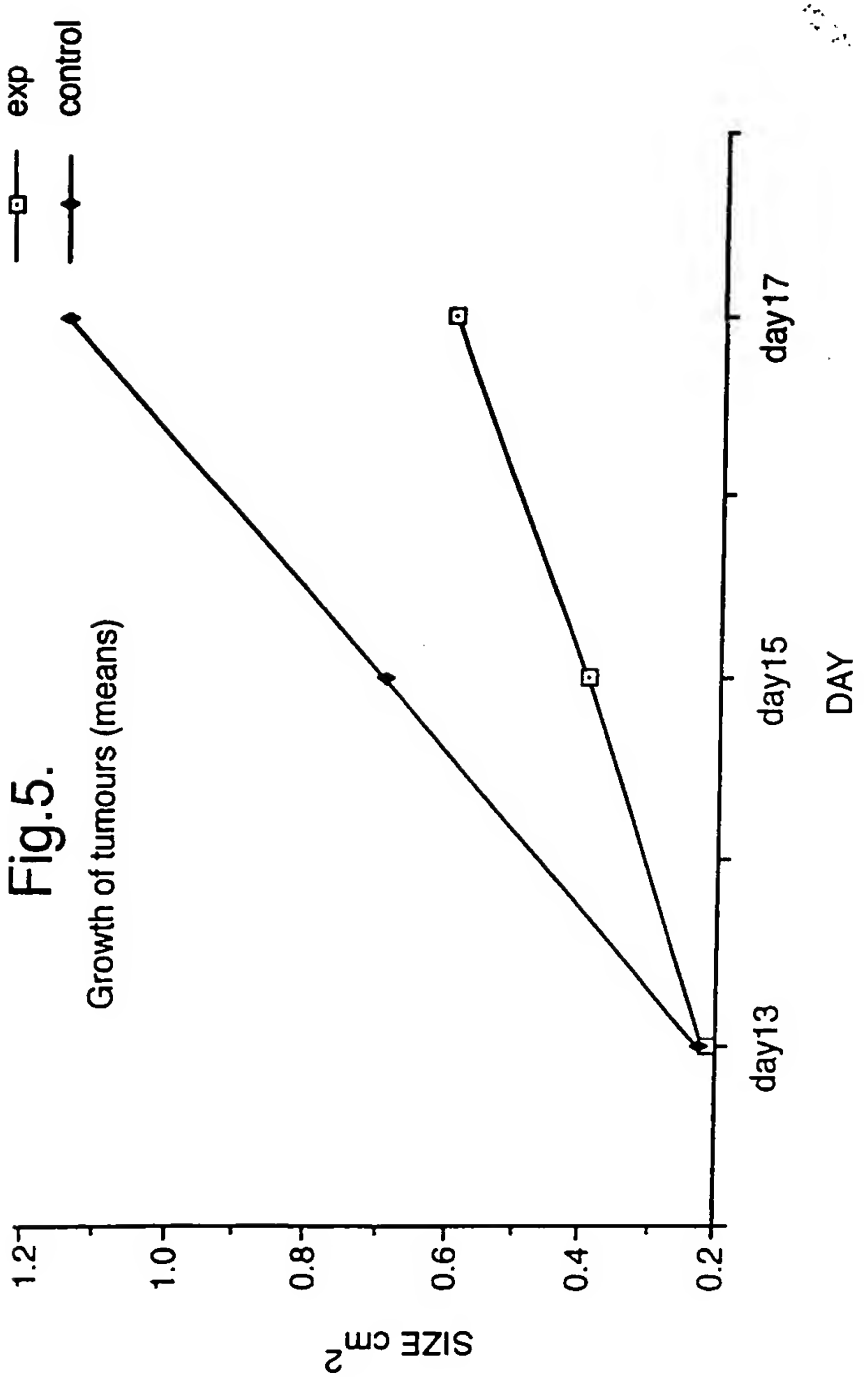

exp
control
Growth of tumours (means)
SIZE cm2
1.2
1.0
0.8
0.6
0.4
0.2
day13
day15
day17
DAY

Fig.5.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
12 April 2001 (12.04.2001)

PCT

(10) International Publication Number
WO 01/24803 A3

(51) International Patent Classification[7]: A61K 33/34, 31/30, 31/60, 31/375, A61P 35/00

(21) International Application Number: PCT/GB00/03770

(22) International Filing Date: 2 October 2000 (02.10.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

9923431.2	4 October 1999 (04.10.1999)	GB
0014420.4	13 June 2000 (13.06.2000)	GB

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
23 August 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/24803 A3

(54) Title: PHARMACEUTICAL COMPOSITIONS CONTAINING COPPER, SALICYLIC ACID AND VITAMINES C

(57) Abstract: A composition comprising: (a) a physiologically acceptable source of assimilable copper; (b) a source of salicylic acid or a physiologically acceptable derivative thereof; and (c) vitamin C.